



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-D-0168]

Benefit-Risk Considerations for Product Quality Assessments; Draft Guidance for Industry;
Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Benefit-Risk Considerations for Product Quality Assessments.” This guidance describes the benefit-risk principles applied by FDA when conducting product quality-related assessments of chemistry, manufacturing, and controls (CMC) information submitted for FDA assessment as part of original new drug applications (NDAs), original biologics license applications (BLAs), or supplements to such applications, in addition to other information (e.g., inspectional findings) available to FDA during its assessment. This guidance discusses how FDA assesses risks, sources of uncertainty, and possible mitigation strategies for a product quality-related issue and how those considerations inform FDA’s understanding of the potential effect on a product. This guidance also discusses how unresolved product quality issues may be addressed in the context of regulatory decision making. The guidance notes that product quality assessments are also done for abbreviated new drug applications (ANDAs), and it discusses how, in certain rare circumstances, unresolved product quality issues may be addressed when there is an urgent clinical need for an ANDA (e.g., a public health emergency or a pervasive drug shortage).

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2022-D-0168 for “Benefit-Risk Considerations for Product Quality Assessments.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document. FOR FURTHER INFORMATION CONTACT: Natalia Comella, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 6648, Silver Spring, MD 20993-0002, 301-796-6226.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Benefit-Risk Considerations for Product Quality Assessments.” This guidance describes the benefit-risk principles applied by FDA when conducting product quality-related assessments of CMC information submitted for FDA assessment as part of original NDAs under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), original BLAs under section 351 of the Public Health Service Act (42 U.S.C. 262), or supplements to such applications, in addition to other information (e.g., inspectional findings) available to FDA during its assessment. This guidance discusses how FDA assesses risks, sources of uncertainty, and possible mitigation strategies for a product quality-related issue and how those considerations inform FDA’s

understanding of the potential effect on a product. The outcome of the product quality assessment results in a determination as to whether an applicant has developed a drug product, manufacturing process, and control strategy that will consistently result in a product of acceptable quality when manufactured at the facilities named in the application.

When a regulatory decision regarding the approval of an NDA or BLA is made, FDA considers the overall benefit(s) and risks identified for the product. This can include any residual risk related to unresolved product quality issues if they directly affect the assessment. This guidance also discusses how unresolved product quality issues may be addressed in the context of regulatory decision making. The guidance notes that product quality assessments are also done for ANDAs, and it discusses how, in certain rare circumstances, unresolved product quality issues may be addressed when there is an urgent clinical need for an ANDA (e.g., a public health emergency or a pervasive drug shortage).

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Benefit-Risk Considerations for Product Quality Assessments." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001; and the collections of

information in 21 CFR parts 601 and 610 have been approved under OMB control number 0910-0338.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: May 5, 2022.

Lauren K. Roth,

Associate Commissioner for Policy.

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